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Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for all designations*
- *of inventorship (Rule 4.17(iv)) for US only*

Published:

- *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **A NOVEL AMORPHOUS FORM OF VALSARTAN**

(57) Abstract: The present invention relates to a novel amorphous form of valsartan, to a process for its preparation and to a pharmaceutical composition containing it.

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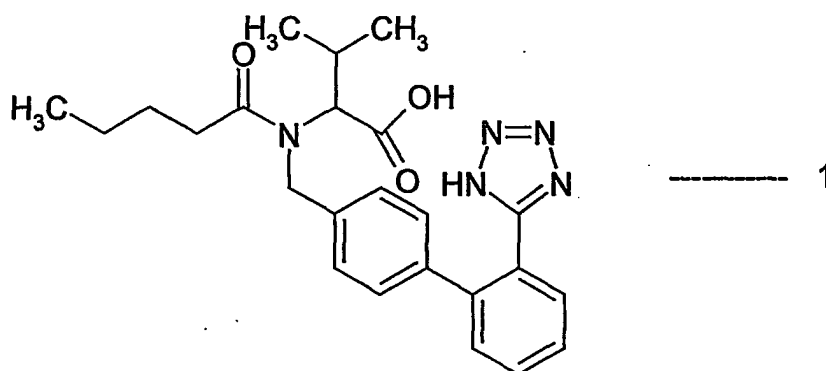
A NOVEL AMORPHOUS FORM OF VALSARTAN

FIELD OF THE INVENTION

5 The present invention relates to a novel amorphous form of valsartan, to a process for its preparation and to a pharmaceutical composition containing it.

BACKGROUND OF THE INVENTION

10 Valsartan of formula (1):



or N-(1-Oxopentyl)-N-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-L-valine, is
15 an antihypertensive agent and its therapeutic uses are disclosed in US
5,399,578. No polymorphs of valsartan is reported in the literature.

We discovered a sufficiently stable amorphous form of valsartan, which
is found to be suitable for pharmaceutical composition.

The object of the present invention is to provide a novel stable
20 amorphous form of valsartan, process the preparing it and a pharmaceutical
composition containing it.

DETAILED DESCRIPTION OF THE INVENTION

25 The present invention provides a novel amorphous form of valsartan
(hereinafter referred to as amorphous valsartan). The amorphous valsartan is
characterized by having broad x-ray diffraction spectrum as in figure 1.

A further aspect of the present invention provides a process for the preparation of amorphous valsartan. Amorphous valsartan is prepared by dissolving valsartan in an alcohol or a mixture of alcohols. The alcohol is selected from the group consisting of methanol, ethanol, isopropyl alcohol, tert-butyl alcohol and n-butyl alcohol. The solvent may be removed from the solution by vacuum drying or spray drying.

A further aspect of the present invention provides a pharmaceutical composition comprising amorphous valsartan and a pharmaceutically acceptable carrier.

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BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a x-ray powder diffraction spectrum of amorphous valsartan.

x-Ray powder diffraction spectrum was measured on a Siemens D5000 x-ray powder diffractometer having a copper-K α radiation.

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The following examples further illustrate the invention.

Example 1

Valsartan (10 gm), (obtained by the process described in example-16 of US 5,399,578) is dissolved in methanol (50 ml). The solution is subjected to vacuum drying at about 40°C for 10 hours to give 9.8 gm of amorphous valsartan.

20

Example 2

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Example 1 is repeated by subjecting the solution to spray drying instead of vacuum drying to give amorphous valsartan.

Example 3

Valsartan (10 gm), (obtained by the process described in example-16 of US 5,399,578) is dissolved in ethanol (60 ml). The solution is subjected to vacuum drying at about 45°C for 12 hours to give 9.7 gm of amorphous valsartan.

30

Example 4

Example 3 is repeated by subjecting the solution to spray drying instead of vacuum drying to give amorphous valsartan.

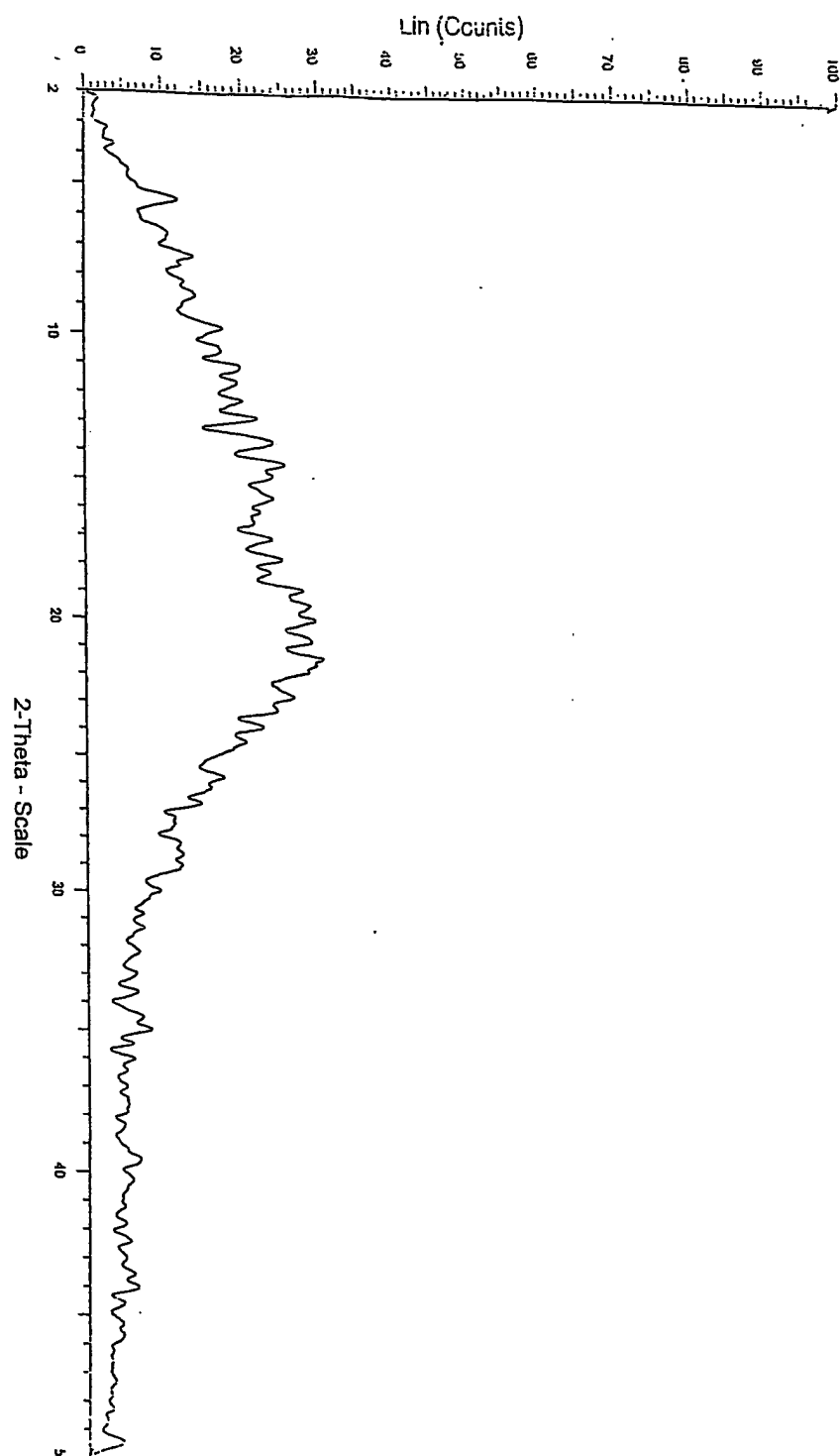
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Example 5

Valsartan (10 gm) is dissolved in isopropyl alcohol (70 ml). The solution is subjected to vacuum drying at about 45°C for 15 hours to give 9.9 gm of amorphous valsartan.

We claim:

1. Amorphous valsartan characterized by an x-ray powder diffraction spectrum as in figure 1.
- 5 2. A process for preparation of amorphous valsartan of claim 1, which comprises:
 - a) dissolving valsartan in an alcohol or a mixture of alcohols;
 - b) removing the solvents from the solution formed in step (a) either by vacuum drying or by spray drying;
- 10 wherein the alcohol is selected from the group consisting of methanol, ethanol isopropyl alcohol, tert-butyl alcohol and n-butyl alcohol.
3. A process according to claim 3, wherein the solvent is removed by vacuum drying.
4. A process according to claim 3, wherein the solvent is removed by spray
15 drying.
5. A pharmaceutical composition comprising amorphous valsartan and a pharmaceutically acceptable carrier.



INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN 03/00096-0

CLASSIFICATION OF SUBJECT MATTER

IPC⁷: C07D 257/04, A61K 31/41

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC⁷: C07D, A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

REGISTRY, CAPLUS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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A	WO 2002/006253 A1 (Novartis A.-G.) 24 January 2002 (24.01.02) <i>abstract.</i>	1-5
A	CN 1317485 A (Pharmaceutical Co., Ltd., Changzhou Pharmaceutical Factory No.4, Peop. Rep. China) 17 October 2001 (17.10.01) <i>abstract.</i>	1-5

☒ Further documents are listed in the continuation of Box C.☒ See patent family annex.

* Special categories of cited documents:

„A“ document defining the general state of the art which is not considered to be of particular relevance

„E“ earlier application or patent but published on or after the international filing date

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„&“ document member of the same patent family

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Name and mailing address of the ISA/AT

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>Jia, Qingzhong; Ma, Guilin; Li, Wenzhi; Jiang, Shaohao "Synthesis of antihypertensive drug valsartan"Zhongguo Yiyao Gongye Zazhi (2001), 32(9), 385-387 CODEN: ZYGZEA; ISSN: 1001-8255 (abstract). Chemical Abstracts [online] Copyright 2003 American Chemical Society [retrieved on 12 August 2003 (12.08.03)]. Retrieved from STN International, Karlsruhe. Chem. Abstr. No. 2001:807594 CAPLUS; abstract. <i>abstract.</i></p> <p style="text-align: center;">---</p>	1-5

INTERNATIONAL SEARCH REPORT

International application No.

Information on patent family members

PCT/IN 03/00096-0

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